GSK Biologicals perspectives on the future IPV

« Polio immunization: moving forward » September 19-20, 2007

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1) Sabin IPV : GSK's position

- sIPV feasibility was assessed at 10 L fermentor scale, using the GSK Bio IPV process and the current Sabin strains

- The 10 L scale studies (2-3 exp for each serotype) demonstrated
  - For T3 : no drift in the neurovirulence profile (Maprec) in our process conditions
  - antigen recovery upon purification similar to current IPV
  - Same inactivation kinetic as the current IPV
  - No loss of the selected MoAb
  - Modified production yield as compared to current IPV

sIPV IN COMPARISON WITH IPV	T1	T2	T3
1. In vitro yield (D antigen)	70%	60%	100%
2. In vivo response (seroneutralization assay in rat using Salk strain for the challenge)	130%	15%	15%

40-8-32 Du → 30-45-200 Du

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1) Sabin IPV : GSK's position

- Based upon:
  - The current IPV dose profile (40-8-32 DU)
  - The yields obtained from 10 L fermentor studies
  - The current IPV production parameters :production scheme, holding times equipment life-times, …
  - The global IPV demand

- Can Sabin IPV be considered a viable industrial alternative?

  → **"NO"** due to significant reduction of the production capacity (25% to 30% of the existing capacity) and given the expected global IPV demand

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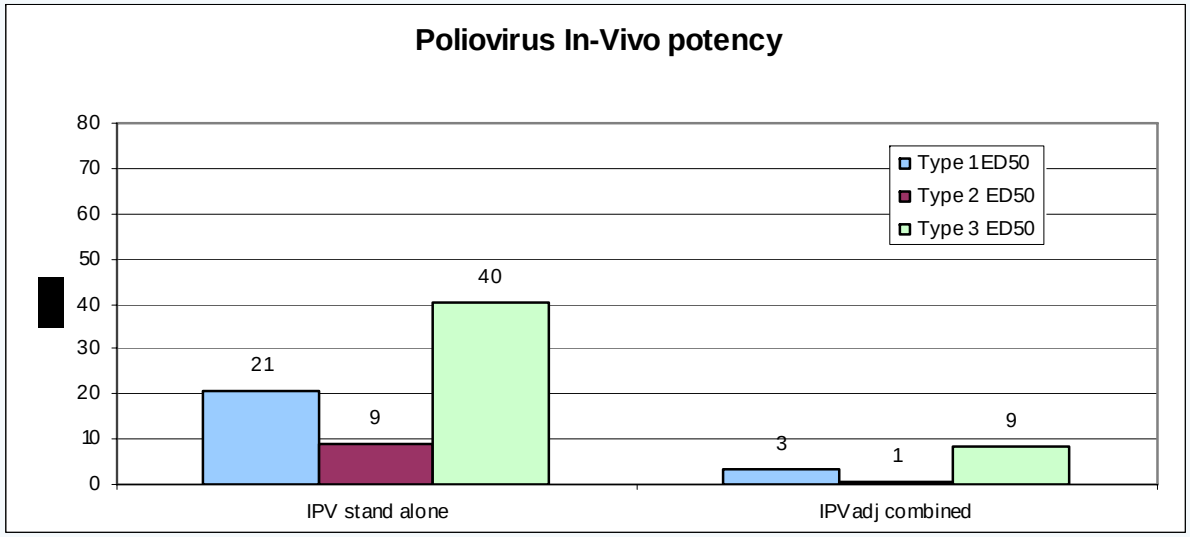
2) Current IPV formulation and potential perspectives

- **In the early 80's**: development of the IPV (2nd generation) based upon the work of RIVM (Van Wezel).
  - Stand alone IPV, formulated on a 40-8-32 DU basis in order to have a vaccine profile able to compete with the oral vaccine

- **In the 90's** : development of IPV combined vaccines (DTPa IPV)
  - Aluminium adsorbed vaccines, formulated on a 40-8-32 DU basis



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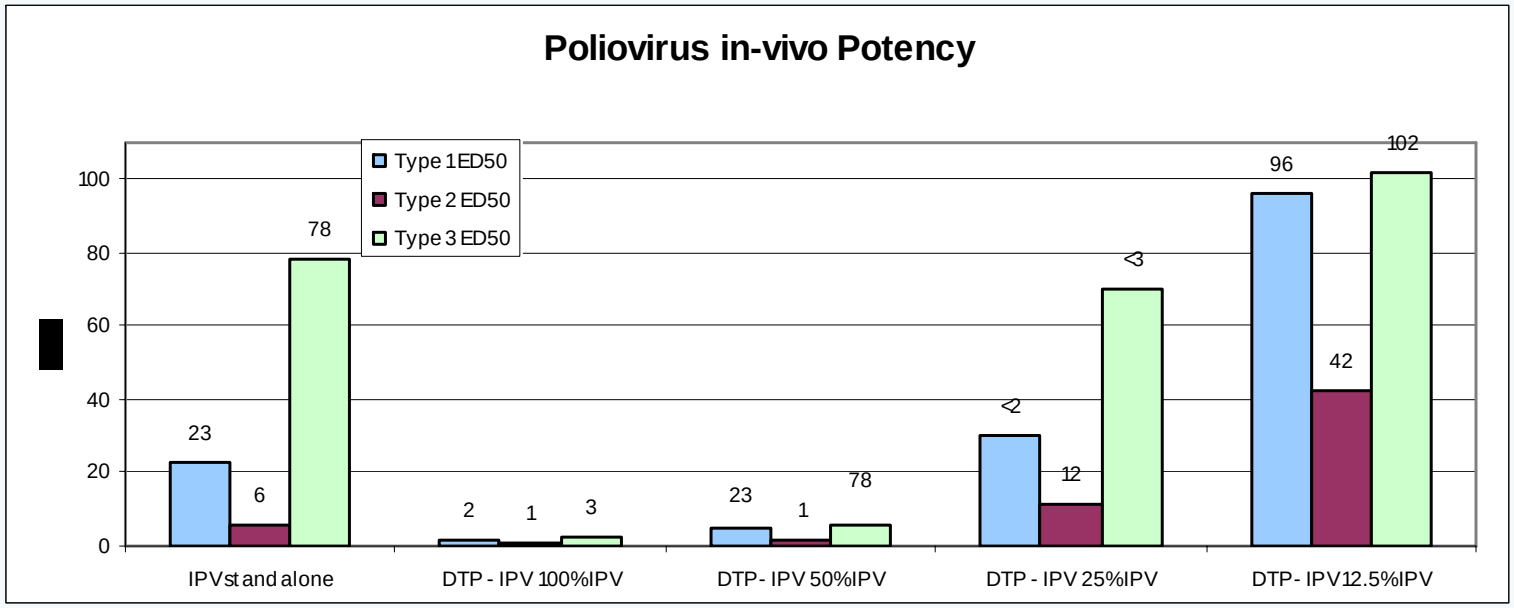
2) Current IPV formulation and potential perspectives

- **In the 2000's :** based on this considerable difference between adjuvanted and stand alone vaccines, and on the high clinical response obtained with the combined vaccines, GSK decided to explore the feasibility of reducing the IPV formulation
  - Aluminium adsorbed vaccines, formulated with ½, ¼, 1/8 IPV dose



→ When IPV is included in a combined vaccine, the presence of adjuvant significantly boosts the immune response and would allow a substantial reduction of the Ag content per dose

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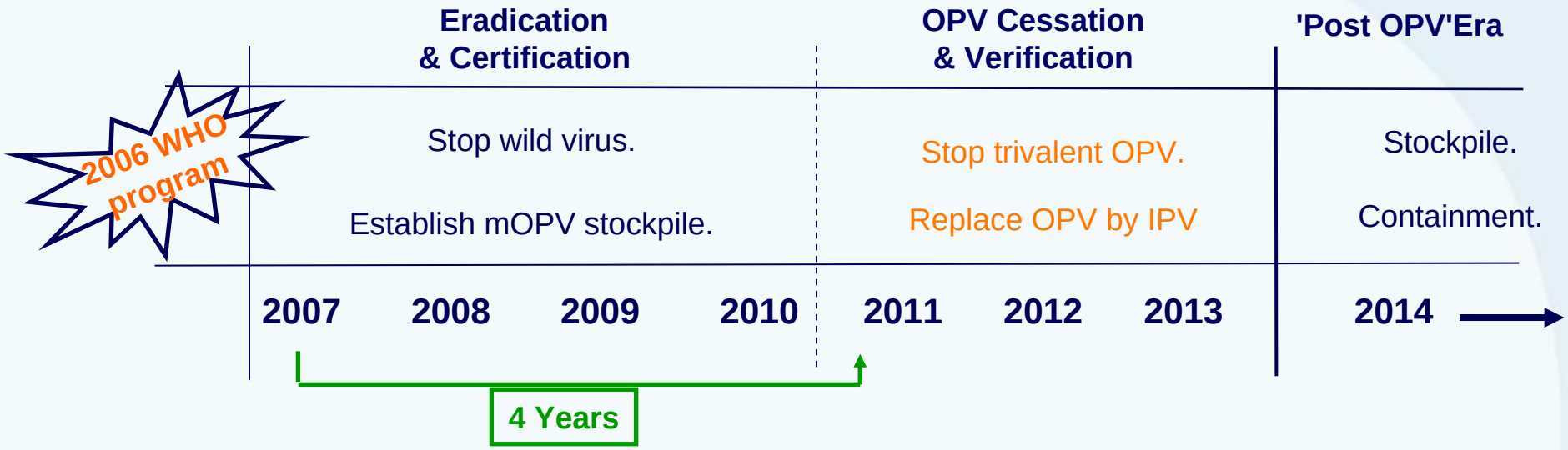
3) Which IPV to fit with the WHO eradication program ?



New IPV vaccines (sIPV, new IPV strain, new adjuvant)

= full clinical package → min 5 years

Build additional IPV capacity (to cope with the global demand)

= facility available & validated → 5 years

= production of consistency lots → 1 year

Regulatory actions →1 – 2 years

Industrial solution → 7 – 8 years

3) Which IPV to fit with the WHO eradication program ?

→ The analysis of the WHO polio eradication program and the manufacturing / regulatory timings clearly demonstrates :

- The urgency to make firm recommendation regarding THE polio vaccine to be available at OPV cessation
- The urgency to allocate industrial and clinical resources
- Timewise, the advantage of capitalizing on the existing vaccines (→adjuvanted IPV in combined vaccines)

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